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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/312,596	05/14/1999	LORNA W. ROLE	46839-B/JPW/	2831

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JOHN P WHITE
COOPER & DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER
GUCKER, STEPHEN

ART UNIT	PAPER NUMBER
1647	15

DATE MAILED: 02/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/312,596	Role et al.
Examiner	**Group Art Unit**
Stephen Rucker	1647

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 12/11/01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-29 is/are pending in the application.

Of the above claim(s) 1-19 + 25-29 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 20-24 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Applicati n Papers

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☑ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 10

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☑ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Acti n Summary

Part III DETAILED ACTION

1. Applicant's election with traverse of Group V, claims 20-24 in Paper No. 14, filed 12/11/01 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I-V are not "independent". Furthermore, Applicants assert that there exists no search burden. This is not persuasive because modern patent practice has long recognized that restriction between even two dependent groups is proper when two or more inventions are distinct and the instant inventions of Groups I-V are distinct.. See M.P.E.P. 802.01. Elected Group V claims are drawn to assays of ligand binding which are patentably separate and distinct from assays for diagnosing a particular disease or predisposition for a particular disease (Group I), a process of maintaining synaptic connections (Group II), methods of therapy (Group III), or a process for inducing neuronal differentiation (Group IV). All of these inventions employ different reagents, different process steps, and are practiced for materially different purposes, and are therefore distinct inventions, one from the other. Furthermore, a search burden exists because prior art relating to these distinct inventions is not co-extensive or even overlapping from one invention to the other because of this distinctness. Finally, the issues such as enablement relating to the multiple inventions are indeed separate and will require separate consideration by the Examiner, adding to the search burden.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-19 and 25-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **with** traverse in Paper No. 14.

3. The abstract of the disclosure is objected to because it is over 150 words in length. Correction is required. See MPEP § 608.01(b).

4. The specification is objected to as the Brief Description of the Drawings section of the application only contains descriptions for Figures 1-19. Page 15 indicates that other drawings exist, but they are not labeled as Figures and no description exists for these drawings as indicated on page 65.

In addition, portions of pages 72-74 of the specification are unintelligible due to the handwritten markings over these pages. These markings are objected to as not being in compliance with 37 CFR 1.52(c) because they are not dated or initialed.

Pages 68-130 are objected to as they do not conform with 37 CRF 1.52(a) and (b). A substitute specification is required to be submitted.

Pages 68-130 are objected to as the references made to figures therein do not correspond to Figures 1-19 submitted by Applicants. Appropriate correction is required.

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent

Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Applicant is given THREE MONTHS from the mailing date of this communication within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 20-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods employing nARIA polypeptide sufficiently characterized by physical or chemical structure, such as by SEQ ID NO, does not reasonably provide enablement for methods employing "nARIA polypeptide". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The disclosure does not contain an adequate written description, examples, or guidance by which methods employing "nARIA polypeptide" characterized only by the verbal phrase "nARIA polypeptide" could be placed into

the hands of the skilled artisan with a reasonable expectation of success without requiring undue experimentation for the following reasons. The scope of "nARIA polypeptide" is defined in the specification as including "amino acid variants of nARIA which are prepared by introducing appropriate nucleotide changes into nARIA nucleic acid or by *in vitro* synthesis of the desired nARIA polypeptide. Such variants include, for example, deletions from, or insertions or substitutions of, residues within the amino acid sequence shown for human nARIA sequence. Any combination of deletions, insertion, and substitution can be made to arrive at the final construct, provided that the final construct possesses the desired characteristics" (page 17, line 35 to page 18, line 7). Because of the unpredictability of the protein arts (see Rudinger, especially page 6), the skilled artisan cannot make and use the broad genus of "nARIA polypeptide" recited in the method claims because such a genus encompasses an unlimited and thereby infinite plurality of amino acid substitutions, deletions, additions, or combinations thereof as compared with the working embodiments because the disclosure does not adequately describe, provide guidance, or give examples of all the critical amino acid residues that bestow upon the protein its "desired characteristics". The instant process claims encompass all types and manner of "nARIA polypeptide,"including synthetic muteins made by genetic engineering, every and all "nARIA polypeptide"from every animal species on earth, and every possible allelic variant of the foregoing, that are not envisioned or adequately described by the disclosure. The working embodiments of the specification are a minor portion of a very broad genus and do not teach or support the majority of the genus as a whole because such a broad and varied genus drawn solely

to the biological functionality of the product used without regard or limitation to its chemical structure cannot be adequately enabled from the few examples taught. See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

8. Claims 20-24 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed "nARIA polypeptide" used in the process claims and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of manufacturing or testing the claimed processes. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable

due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. (See page 1115.).

It is suggested that by limiting the claims to methods using the instant "nARIA polypeptide" described as a SEQ ID NO would obviate the grounds of this rejection.

9. Claims 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is vague and unclear if the "receptor-affinity derivative" recited in base claim 20 is a receptor-affinity derivative for the compound being tested for the modulation of binding of nARIA polypeptide or for the nARIA polypeptide-affinity derivative. Additionally, if the compound is merely and solely incubated with an "appropriate nARIA polypeptide-affinity derivative" as is encompassed by the claim, it is vague and unclear how an artisan can determine if said compound is capable of modulating the binding of an nARIA polypeptide to its receptor since no receptor is then recited in the body of the claim.

10. Applicant is advised that should claim 21 be found allowable, claim 22 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
>
> (f) he did not himself invent the subject matter sought to be patented.

12. Claims 20 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Goodearl et al. (US 5,602,096, "Goodearl"). Goodearl discloses glial growth factors (GGF) that possess nARIA activity in that they induce acetylcholine receptor synthesis by binding to the same receptor ($p185^{erbB2}$ or erbB2) as does "nARIA polypeptide" (abstract, column 5, line 36; column 16, line 65 to column 17, line 5; column 47, lines 5-17; and claims 1-2.). Goodearl also discloses competitive assays with glial growth factors and antibodies which meet the limitations of the claims (column 4, lines 63 to column 5, line 7; column 12, lines 19-23 and lines 44-50; column 8, lines 16-57). It is noted that the claims as presently written do not require the presence of a receptor, but only a ligand (an ARIA or a GGF) and an antibody.

13. Claims 20-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Role (US 6,284,535 B1, "Role"). Role discloses the invention at column 16, line 61 to column 17, line 13.

14. Claims 20-24 are rejected under 35 U.S.C. 102(f) because some of the applicants did not invent the claimed subject matter. The invention is disclosed in its entirety and verbatim in the

Role patent at column 16, line 61 to column 17, line 13. Compare page 35, line 29 to page 36, line 13 of the instant application with column 16, line 61 to column 17, line 13 of the Role patent. Lorna W. Role is listed as the sole inventor of US 6,284,535 B1. Therefore, applicants David Talmage and Jianxin Bao of the instant application are not co-inventors of the invention sought to be patented in the instant application.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodearl in view of Role. The teachings of Goodearl are as set forth in ¶**11** above. Goodearl does not teach the affinity complex comprising an nARIA receptor bound to an affinity derivative or specific affinity derivatives. Role teaches the affinity complex comprising an nARIA receptor bound to

an affinity derivative or specific affinity derivatives at column 16, line 61 to column 17, line 13. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the methods of Goodearl with the methods of Role because both US patents have a common nexus of teaching the inducement of ACh receptors by the use of nARIA or GGF (which are alternately spliced from the same gene and act on the same receptor), both patents disclose competitive binding assays and antibodies using nARIA or GGF, and the use of affinity derivatives such as sepharose is common practice in the art for competitive binding assays such as immunoassays and ELISAs because of the advantage of having a ligand or receptor reagent bound to an affinity derivative such as sepharose for the convenience of making said assay amenable to being used, sold, or marketed in kit form.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (703) 308-6571. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is currently (703) 308-4242, but Applicant should confirm this by phoning the Examiner before faxing.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SG

Stephen Gucker

February 24, 2002

Gary L. Kunz

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600